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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	PAPER NUMBER
	4

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/166,649	Schmidt et al.
Examiner	**Group Art Unit**
Eileen B. O'Hara	1646

X Responsive to communication(s) filed on *Sept. 14, 1999 and April 13, 2000*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

X Claim(s) *1-57* is/are pending in the applicat

Of the above, claim(s) *3, 9, 10, 14, 16, 19, 23, and 30-57* is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

X Claim(s) *1, 2, 4-8, 11-13, 15, 17, 18, 20-22, and 24-29* is/are rejected.

☐ Claim(s) _____ is/are objected to.

X Claims *1-57* ~~are~~ *was* subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

X Notice of References Cited, PTO-892

X Information Disclosure Statement(s), PTO-1449, Paper No(s). *4*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. Claims 1-57 are pending in the instant application.

Election/Restriction

2. Applicant's election with traverse of Group I, claims 1-13 and 15-29 in Paper No. 6 is acknowledged. The traversal is on the ground(s) that it would not be a burden for the Examiner to search Groups I-IV together since such groups do not define distinct inventions, and a search of the prior art for the subject matter defined by the claims in any one of Groups I-IV would necessarily overlap and possibly identify art pertaining to the subject matter defined by claims in any of the other Groups. This is not found persuasive because:

Under MPEP § 803, there are two criteria for a proper requirement for restriction between patentably distinct inventions:

(A) The inventions must be independent (see MPEP § 8702.01, 806.04, 808.01) **or** distinct as claimed (see MPEP § 806.05 - § 806.05(I): and

(B) There must be a serious burden on the examiner if restriction is required (see MPEP § 803.02, § 806.04(a) - § 806.04(I), § 808.01(a), and § 808.02).

The term "distinct" means that two or more subjects as disclosed are related, for example, as combination and part (subcombination) thereof, process and apparatus for its practice, process and product made, etc., but are capable of separate manufacture, use or sale as claimed, **and are patentable** (novel and unobvious) **over each other** (though they may each be unpatentable because of the prior art). It will be noted that in this definition the term related is used as an

alternative for dependent in referring to subjects other than independent subjects. (MPEP § 802.01). Where inventions are related as disclosed but are distinct as claimed, restriction may be proper (MPEP § 806(B)). In the instant case the four inventions are related but distinct.

Consistent with current patent practice, a serious search burden may be established by (A) separate classification thereof: (B) a separate status in the art when they are classifiable together: (C) a different field of search:. The four inventions, though related, would require non-coextensive literature searches. Further, a search is directed not only to art which would be anticipatory, but also to art that would render the invention obvious. Thus, the four groups require divergent searches, and to search all four inventions would be burdensome. Therefore, the restriction is maintained.

The requirement is still deemed proper and is therefore made FINAL.

Species Election

3. Applicant's election of the following species in Paper No. 8, filed April 13, 2000 is acknowledged: (a) peptide: carboxymethyl-lysine modified; (b) derivatization of the peptide: alkyl; and (c) compound: polypeptide.

4. Claims 3, 9, 10, 14, 16, 19, 23 and 30-57 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 6.

5. Claims 1, 2, 4-8, 11-13, 15, 17, 18, 20-22 and 24-29 will be prosecuted on the merits.

Specification

6.0 The disclosure is objected to because of the following informalities:

6.1 The word polypeptide on page 9, line 10 is misspelled.

6.2 On page 13, line 3, the last word "pepetide" is misspelled.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1, 2, 4-8, 11-13, 15, 17, 18, 20-22 and 24-29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for determining whether a compound is capable of inhibiting the interaction of a peptide with a receptor for advanced glycation end product (RAGE) using the full length receptor or the V-domain of the receptor, does not reasonably provide enablement for any other receptor fragment. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claims encompass a competitive binding assay using RAGE, or a fragment of RAGE. On page 8, lines 11-21 of the instant specification, a fragment of RAGE is defined as being at

least 5 amino acids in length. The specification teaches that the V-domain of RAGE, comprising amino acids 1-120 of the full length protein (which is 404 amino acids in length), and soluble RAGE, comprising the extracellular two-thirds of the amino acid sequence of membrane-bound RAGE, can bind to various advanced glycation end products such as CML-BSA and be used in a competitive binding assay. However, given that a fragment of RAGE can be as small as 5 amino acids in length, and that the disclosure does not provide examples of experiments using RAGE fragments smaller than the V-domain or sRAGE, one of skill in the art would not expect a fragment as small as 5 amino acids to be capable of binding an advanced glycation end product and so be useful in the assay.

This rejection could be overcome by insertion of a functional limitation in claim 1, such as, for example in section (a) (ii): "RAGE or a fragment of RAGE that can bind the peptide".

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claim 18 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 18 is indefinite because "polyepetide" is not a word.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

9.1 Claims 1, 2, 5-8, 13, 15, 17, 18, 20-22 and 24-28 are rejected under 35 U.S.C. 102(e) as being anticipated by Morser et al., PN 5,864,018, filing date April 16, 1996.

Claims 1, 2, 5-8, 13, 15, 17, 18, 20-22 and 24-28 encompass a method for determining whether a compound is capable of inhibiting the interaction of a peptide with a receptor for advanced glycation end product (RAGE) in a competitive assay, comprising admixing the peptide (wherein the amino groups are inactivated by chemical derivatization) with RAGE or a fragment of RAGE in the presence and the absence of the compound, wherein the peptide is an AGE or fragment thereof that is carboxymethly-lysine, modified, synthetic, the peptide is derivatized via chemical modification resulting in an alkyl derivative or is synthetic, and wherein the RAGE or RAGE fragment is synthetic, soluble or comprises the V-domain, wherein the compound is sRAGE, a polypeptide, a polyclonal or monoclonal, humanized, chimeric or privatized antibody, and wherein the peptide or RAGE is affixed to a solid surface, and the peptide or RAGE is labeled.

Morser et al. teach a method of using the AGE/RAGE interaction in order to screen test compounds in order to identify agonists or antagonists of the AGE/RAGE interaction. In column 16, line 29 to column 17, line 54, Morser et al. teaches that test compounds may be chemical compounds, biological macromolecules, or extracts made from biological materials such as bacteria, plants, fungi, or animal cells or tissues, and test compounds will typically include the polypeptides or fragments of the present invention (AGEs and RAGE or sRAGE or RAGE fragment) as well as structural analogs or peptidomimetics which are derived from these polypeptides or the antibodies described in the patent, and substrates or ligands thereof (column 16, lines 35-44).

In column 16, line 50 to column 17, line 35, Morser et al. teach that the screening methods typically involve incubation of RAGE with an advanced glycoslylation end-product protein (AGE, a derivatized, inactivated protein) such as AGE-BSA, nonenzymatically N-glycosylated collagen, myelin or the like, as well as the test compound, and that typically, one of the RAGE polypeptide or AGE will be immobilized upon a solid support which will then be contacted with the other protein or peptide, and that the one of the pair will include a labeling group such as radiolabels, chemiluminescent or fluorescent groups (column 9, lines 44-54).

In column 5, lines 24-28, Morser et al. teach that the soluble RAGE polypeptides generally comprise fragments of the extracellular domain of RAGE, and the soluble peptides will comprise one or more of the IG-like domains of the extracellular region of RAGE (the V-domain). In column 6, lines 41-52, Morser et al. also teach that the polypeptides may also be

characterized by their ability to block the interaction between two proteins, and include peptides derived from RAGE such as fragments which encompass AGE binding regions of RAGE as well as AGE-binding proteins.

In column 5, lines 33-38, Morser et al. teach that the polypeptides may be characterized by their ability to either mimic or inhibit the interaction between AGEs and their receptors (RAGE), and that those polypeptides which are mimetic of either AGE or its receptors in the AGE/receptor interaction are termed AGE or AGE receptor "mimics".

Morser et al. in column 10, line 6 to column 11, line 56 teach antibodies that bind with relative high affinity to RAGE, and can be used for a number of purposes, including inhibiting interaction between AGEs and their receptors, and that these antibodies can be monoclonal, polyclonal, fragments, chimeric or humanized. In column 7, lines 22-35, Morser et al. teaches that the polypeptides of the invention may be prepared using synthetic methods.

Therefore, from the teachings of Morser et al., claims 1, 2, 5-8, 11-13, 15, 17, 18, 20-22 and 24-28 are anticipated.

9.2 Claim 29 is rejected under 35 U.S.C. 102(b) as being clearly anticipated by Stern et al., WO 97/26913, July 31, 1997.

Claim 29 encompasses a method for determining whether a compound is capable of inhibiting the interaction of a peptide with a receptor for advanced glycation end product (RAGE) in a competitive assay, comprising admixing the peptide (wherein the amino groups are

inactivated by chemical derivatization) with RAGE or a fragment of RAGE in the presence and the absence of the compound, and wherein the assay occurs in a cell.

Stern et al. teach a method for evaluating the ability of an agent to inhibit binding of an amyloid-β peptide (derivatized, inactivated peptide) with a receptor for advanced glycation end product on the surface of a cell which includes contacting the cell with the agent and amyloid-β peptide, determining the amount of amyloid-β peptide bound to the cell and comparing the amount of bound amyloid-β peptide with the amount determined in the absence of the agent (see abstract, page 3, page 13 and claims 49-51.

Therefore, Stern et al. clearly anticipates claim 29.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10.1 Claims 4, 11 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morser et al. and further in view of Reddy et al., Biochemistry, Vol.34, pp 10872-10878, 1995 (cited in IDS).

The teachings of Morser et al. are described above. Morser et al. differs from claims 4, 11 and 12 in that they do not specifically teach carboxymethly-lysine-modified peptides in the assay method.

Reddy et al. teaches that carboxymethly-lysine is a dominant advanced glycation end product (AGE) antigen in proteins.

Given that carboxymethyl-lysine-modified peptides are a dominant AGE, it would have been *prima facie* obvious to one of skill in the art of AGE/RAGE art at the time of the invention to use a carboxymethly-lysine-modified peptide of Reddy as the AGE in the AGE/RAGE competition assay of Morser et al. to determine whether a compound is capable of inhibiting the AGE/RAGE interaction. Morser et al. teaches that since AGES have been implicated in a variety of disorders including complications associated with diabetes and normal aging, and because of the effects AGEs may have in the pathogenesis of a number of disorders, it would generally be desirable to provide compositions and methods to block or otherwise inhibit these effects, and particularly the interaction between AGEs and their cell surface receptors (columns 1-2).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (703) 308-3312. The examiner can normally be reached on Monday through Friday from 9:00 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (703) 308-6564.

Official papers filed by fax should be directed to (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Eileen B. O'Hara, Ph.D

Eileen B. O'Hara 6/28/00

Patent Examiner

LORRAINE SPECTOR
PRIMARY EXAMINER